A) Scientific Abstract

Several melanoma antigens have been identified and include MAGE 1 and 3, gp100, tyrosinase and MART-1/Melan-A. MART-1 is widely expressed in melanoma and is recognized by the majority of HLA-A2 restricted cytotoxic T lymphcytes (CTL) generated from tumor infiltrating lymphocytes (TIL). An immunodominant peptide derived from the MART-1 118 amino acid protein (13kD) designated $MART_{27-35}$ is expressed by HLA-A2.1 melanoma cells[1]. In addition, peptide $MART_{27-35}$ can be presented by HLA-A2.2, 2.4, 2.5, 2.6, 2.9 and 69.1 major histocompatibility complex subtypes[2].

Peripheral blood mononuclear cells (PBMC) can be differentiated into potent antigen-presenting cells (APC) with dendritic cell (DC) properties following the method of Romani *et al*[3], and these cultured DC have been shown to be superior to other APC for the generation of specific immune effectors. Transfection of a tumor antigen gene into DC would enable a continuous processing and presentation of antigenic peptides in the context of the patient's HLA subtype[4,5,6]. Genetically engineered DC are able to induce specific CTLs with fewer *in vitro* stimulations than when DC are exogenously pulsed with peptides[4,6]. We have constructed a replicant-deficient, E1-deleted adenoviral vector carrying the MART-1 gene (AdVMART1). Transduction of *in vitro* cultured HLA-A2.1 and A2.4 DC with AdVMART1 allows these cells to process and present appropriate MART-1 peptides capable of stimulating MART-1-specific T cells[7,8].

We have also developed a preclinical model using murine tumor cells expressing the MART-1 gene[9]. In this model, AdVMART1-transduced murine DC elicit a strong systemic immune response capable of treating established tumor implants. The observed response is MHC class I-restricted and MART-1-specific as assessed *in vitro* and *in vivo*. Our murine model suggests that the ability to generate CTL with MART-1-expressing human DC will have therapeutic benefit in the treatment of cancer subjects.

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